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10/524,754

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EXAMINER

WHALEY, PABLO S

ART UNIT

PAPER NUMBER

1631

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/524,754	Applicant(s) KASABOV ET AL.	
	Examiner PABLO WHALEY	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 June 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 8-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 8-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1631

DETAILED ACTION

Claims Under Examination

Claims 1-6 and 8-17 are under examination. Claim 7 is cancelled.

Priority

This application has been granted the benefit of priority to U.S. Provisional Application No. 60/403,756, filed Aug. 15, 2002.

Withdrawn Rejections

The rejection of claims 1-6 and 8-17 are rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement, is withdrawn in view of applicant's amendments, filed 06/06/2008.

The rejection of claims 1-6 and 8-17 under 35 U.S.C. 103(a) as being unpatentable over Downs in view of Ben-Dor, is withdrawn in view of applicant's amendments, filed 06/06/2008.

The rejection of claims 1-3, 5, 6, 8-10, and 13-15 under 35 U.S.C. 103(a) as being unpatentable over Bagne in view of Slonim, is withdrawn in view of applicant's amendments, filed 06/06/2008.

Art Unit: 1631

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 and 8-17 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. These claims are rejected for the following reasons.

Claims 1-6, and 8-12 are drawn to a system for carrying out a process. For a process to be statutory, it must provide: (1) a practical application by physical transformation (i.e. reduction of an article to a different state or thing), or (2) a practical application that produces a concrete, tangible, and useful result [State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998)], [AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999))]. As noted in State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), the statutory category of the claimed subject matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result. The question of whether a claim encompasses statutory subject matter should not focus on which of the four categories of subject matter a claim is directed to a process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility. Therefore, for a system that carries out a process to be statutory it must also provide a concrete, tangible, and useful result.

In the instant case, the claimed process does not result in a physical transformation of matter. Where a claimed process does not result in a physical transformation of matter, it may be statutory where it recites a result that is concrete (i.e. reproducible), tangible (i.e. communicated to a user), and

Art Unit: 1631

useful result (i.e. a specific and substantial). Claim 1 comprises an output device without explicitly claiming what information is output. Therefore, the process performed by the claimed system lacks a tangible result because nothing is communicated to a user in a user readable format. This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment.

In addition, claims 3 and 4 are non-statutory because they read on abstract ideas. The prohibition on patenting abstract ideas has two distinct aspects: (1) when an abstract concept has no claimed practical application, it is not patentable; (2) while an abstract concept may have a practical application, a claim reciting an algorithm or abstract idea can state statutory subject matter only if it is embodied in, operates on, transforms, or otherwise is tied to another class of statutory subject matter under 35 U.S.C. §101 (i.e. a machine, manufacture, or composition of matter). (See *In re Comiskey*, Fed. Cir., No. 2006-1286, 9/20/07; *Gottschalk v. Benson*, 409 U.S. 63, 175 USPQ 673, 1972).

In the instant case, claims 3 and 4 comprise steps of using modules to carry out processes. The specification does not limit the claimed modules to a machine [p.4 and 5]. Therefore claims 3 and 4 do not qualify as a statutory process because the method steps that are critical to the invention are "not limited to a particular apparatus or machine." To qualify as a statutory process, the critical method steps recited in claims 3 and 4 should positively recite the other statutory class (the thing or product) to which it is tied, for example by identifying the apparatus that accomplishes the method steps, or positively recite the subject matter that is being transformed, for example by identifying the material that is being changed to a different state or thing. Nominal data gathering or post solution activity steps in the claimed subject matter will not be considered sufficient to convert a process that otherwise recites only mental steps into statutory subject matter. Preamble limitations that require the claimed process to comprise machine implemented steps will not be considered sufficient to convert a process that otherwise recites only

Art Unit: 1631

mental steps into statutory subject matter. The applicants are cautioned against introduction of new matter in an amendment.

Response to Arguments

Applicant's arguments filed 06/06/2008, that the amendment of claim 1 to recite "an output device" has been fully considered but is not persuasive for the following reasons. Claim 1 comprises an output device without explicitly claiming what information is output. Therefore, the process performed by the claimed system lacks a tangible result because nothing is communicated to a user in a user readable format. This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. This rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1631

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 and 8-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Downs et al. (Artificial Intelligence in Medicine, 1996, Vol. 8, p.403-428), in view of Barnhill et al. (US 5,769,074; Issued Jun. 23, 1998), and in view of Hemstreet (US 5,733,721; Issued Mar. 31, 1998).

This new a ground of rejection is necessitated by applicant's amendment of claims 1, 2, 3, 5, and 6, filed 06/06/2008.

Downs et al. teach a method and system using an adaptive resonance theory based neural network model (ARTMAP), which is broadly interpreted as an evolving fuzzy neural network, for making classifications and predictions of medical data [Abstract]. In particular, Downs shows a fuzzy ARTMAP voting strategy outcome [p.409, Section 3.2] comprising a number of networks trained on different orderings of the training data; during testing, each individual network makes its prediction for a test item in the normal way; the number of predictions made for each category is then totaled and the one with the highest score (or the most 'votes') is the final predicted category. This voting strategy provides improved performance in comparison to the individual networks. In addition, it also provides an indication of the confidence of a particular prediction, since the larger the voting majority, the more certain is the prediction. The fuzzy ARTMAP consists of 3 modules, 2 fuzzy ART systems, and a related structure

Art Unit: 1631

called the map field [p.406, ¶3 and Fig. 1] and is applied to training and test data sets. Downs shows the use of clinical and electrocardiographic data considered to be useful for patient prognosis [Section 3.1], as well as the use of tissue samples for predicting breast cancer in patients [Section 4.1, p.411]. Downs also employs a 'category pruning' (i.e. decision layer) that functions to improve model specificity based on confidence factors for each classified data cluster, and usage and accuracy scores for each predictive node [Section 4.2.1, p.413]. Downs shows their system can make use of the most highly predictive data (e.g. the ECG codings in the case of myocardial infarction diagnosis) first, and then request additional information on physical signs, associated symptoms, risk factors, clinical history etc (i.e. clinical information) as required, until a confident prediction could be made.

Downs does not teach software to calculate connection weights β_1 , β_2 , and α between Class A and Class B classifier outputs to produce a combined Class A/Class B output according to the following steps: i) assign initial connection weights β_1 , β_2 , and α between 0 and 1 ; ii) calculate Combined Class A output = $(C1/\text{classA} \times \beta_1) + (C2/\text{classA} \times \beta_2)$; iii). calculate Combined Class B output = $(C1/\text{classB} \times (1 - \beta_1)) \times (C2/\text{classB} \times (1 - \beta_2))$; iv). calculate Combined Class A/Class B output = $(\text{Combined Class A output} \times \alpha) + (\text{Combined Class B output} \times (1 - \alpha))$; so that the error of Combined Class A/Class B output is minimized; wherein Class A is a first medical outcome, Class B is a second medical outcome, C1 is classified gene expression data and C2 is classified clinical information; said Combined Class A/Class B output being between 0 and 1 ; and wherein if said Combined Class A/Class B output is closer to 0, said outcome is Class A and wherein if said Combined Class A/Class B output is closer to 1, said outcome is Class B, as in claims 1, 3, and 8.

Downs does not specifically teach a multi-layer preceptron method, as in claims 2 and 6.

Downs does not teach an additional predictor module comprising combined gene expression data and clinical information data, as in claims 5.

Art Unit: 1631

Barnhill teaches a method for predicting medical outcomes including breast cancer [Abstract, Col. 16, line 15]. In particular, Barnhill teaches an arbitrary number of user definable connection weights that are between 0 and 1 and that add up to 1 [Fig. 4 and Col. 17, lines 1-10, and Col. 19, lines 1-10], which makes obvious the use of β_1 , β_2 , and α , as in claims 1, 3, and 8. Barnhill teaches biomarkers and patient data known to be associated with disease (i.e. classified data) [Col. 15, lines 20-65]. Barnhill teaches modules that allow for combining at least two types of input [Col. 14, lines 43-53, Col. 24, Example, part d], which shows the use of combined classification data. Medical outcomes by calculating disease index values using biomarker data and patient information as a linear combination of connection weights [Fig. 4, Col. 13, lines 3-30; Col. 19, lines 44-52], which makes obvious the linear equations based on classified data and weights, as in claims 1 and 3 (steps i-iv). Output values above 0.5 indicate malignant tumors and output values less than 0.5 indicate benign tumors [Col. 17, lines 13-25], which shows combined outcomes closer to 0 and closer to 1. Barnhill teaches adjustment of connection weights and threshold values to reduce classification error [Col. 19, lines 1-10]. Barnhill teaches output values between 0 and 1 [Fig. 5A]. Barnhill teaches methods for minimizing error [Col. 17, lines 50-65, Col. 19, lines 44-52, Fig. 4]. Barnhill teaches a multi-layer perceptron method for statistical validation [Col. 17, lines 33-45], as in claim 2.

Hemstreet teaches a predictive method using classified gene expression data in combination with neural networks and connection weights [Col. 12, Example 1, Fig. 5A, and Col. 37 and 38, Example 6], as in claims 1 and 3. Additionally, Hemstreet also teaches risk assessment by the inclusion of personal data [Col. 36, lines 38-50], which makes obvious the use of an additional module for combining gene expression and clinical data, as in claim 5. The benefit of this method is automated diagnosis using encoded gray level images [Col. 37, lines 29-35].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the invention of Downs as taught above, using the connection weight model taught

Art Unit: 1631

by Barnhill, since the use of connection weights with neural networks for learning is well known in the art, as shown by Downs [p.405, Section 2]. One of ordinary skill in the art would have been motivated to make the above combinations in order to use an automated method for producing and transmitting diagnostic or prognostic values to remote locations, as suggested by Barnhill [Col. 1, lines 20-30].

It would further have obvious to someone of ordinary skill in the art at the time of the instant invention to modify the invention of Downs as taught above, using gene expression data in the predictive model, as taught by Hemstreet, since Barnhill teaches the use of gene marker data [Col. 20, lines 35-40], which makes obvious the use of gene expression data. One of ordinary skill in the art would have been motivated to make the above combinations in order to use an automated method for diagnosis using encoded gray level gene expression images, as suggested by Hemstreet [Col. 37, lines 29-35].

Response to Arguments

Applicant's arguments, filed 06/06/2008, with respect to the rejection of claims 1-6 and 8-17 under 35 U.S.C. 103(a) as being unpatentable over Downs in view of Ben-Dor, have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view applicant's amendments to claims 1, 2, 3, 5, and 6, filed 06/06/2008.

Applicant's arguments, filed 06/06/2008, that the Downs and Ben-dor do not teach any method for increasing the reliability of making a prediction greater than the "most highly predictive data" or to define any criteria by which a "confident prediction" could be made have been fully considered but are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., making a prediction greater than the "most highly predictive data") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the

Art Unit: 1631

claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant's arguments, filed 06/06/2008, with respect to the rejection of claims 1-3, 5, 6, 8-10, and 13-15 under 35 U.S.C. 103(a) as being unpatentable over Bagne in view of Slonim, that the Downs and Ben-dor do not teach steps for minimizing the error of combined classes have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view applicant's amendments to claims 1, 2, 3, 5, and 6, filed 06/06/2008.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1631

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Pablo S. Whaley/

Patent Examiner

Art Unit 1631

/John S. Brusca/

Primary Examiner, Art Unit 1631